

## PATENT COOPERATION TREATY

REC'D 20 MAY 2005


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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 150381/KB	<b>FOR FURTHER ACTION</b> See Form PCT/PEA/416	
International application No. PCT/CZ2004/000050	International filing date (day/month/year) 24.08.2004	Priority date (day/month/year) 26.08.2003
International Patent Classification (IPC) or national classification and IPC C07D491/22		
Applicant PLIVA-LACHEMA A.S. et al.		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>		
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input checked="" type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>		
Date of submission of the demand  21.03.2005	Date of completion of this report  19.05.2005	
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Deutsch, W  Telephone No. +49 89 2399-8281	



**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/CZ2004/000050

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**Box No. 1 Basis of the report**

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1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

- ☐ international search (under Rules 12.3 and 23.1(b))
- ☐ publication of the international application (under Rule 12.4)
- ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

**Description, Pages**

1-4 as originally filed

**Claims, Numbers**

1-5 as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	1-5
	No: Claims	
Inventive step (IS)	Yes: Claims	1-5
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-5
	No: Claims	

**2. Citations and explanations (Rule 70.7):**

**see separate sheet**

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**Box No. VII Certain defects in the international application**

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The following defects in the form or contents of the international application have been noted:

**see separate sheet**

V

Reference is made to the following documents:

- D1: SAWADA, SEIGO ET AL.: "Synthesis and antitumor activity of 20(S)-camptothecin derivatives: carbamate-linked, water soluble derivatives of 7-ethyl-10-hydroxycamptothecin" CHEMICAL AND PHARMACEUTICAL BULLETIN, vol. 39, no. 6, 1991, pages 1446-1454, XP002306175
- D2: US-B-6 235 9071 (HENEGAR KEVIN E ET AL) 22 May 2001 (2001-05-22)
- D3: US-A-4 604 463 (SUGINO EIICHI ET AL) 5 August 1986 (1986-08-05)
- D4: WO 96/31513 A (UPJOHN CO ; HENEGAR KEVIN E (US); SIH JOHN C (US)) 10 October 1996 (1996-10-10)

**Novelty**

The compounds of the present application differ from those disclosed in D1 - D4 through the use of dimethylamino pyridine.

**Inventive Step**

The closest prior art considered to be D1, D2 (see column 23) or D3 (see example 4c).

The only difference between the process of the present claims and those of D1-D3 is the use dimethylaminopyridine for the reaction of the compounds of formula II and III in place of pyridine.

The skilled person would have readily considered replacing pyridine by dimethylaminopyridine (qualitative) and through the polar aprotic solvent.

The problem underlying the invention is provision of a further process for the preparation of irinotecan base having surprising effects compared to the closest prior art.

The present process allows simpler "work ups" compared to the processes of the prior art

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(SEPARATE SHEET)**

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involving pyridine and gives rise to considerably higher yields than the prior art processes (cf page 2, line 6 in the description of the present application and example 1 of the application). The skilled person would not have considered that dimethylaminopyridine and polar aprotic solvent could be used to achieve these effects, such that an inventive step may be acknowledged.

**VII**

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D4 are not mentioned in the description, nor is/are these documents identified therein.

**Box No. VIII (iv) DECLARATION: INVENTORSHIP** (only for the purposes of the designation of the United States of America)  
*The declaration must conform to the following standardized wording provided for in Section 214; see Notes to Boxes Nos. VIII, VIII (i) to (v) (in general) and the specific Notes to Box No. VIII (iv). If this Box is not used, this sheet should not be included in the request.*

**Declaration of inventorship (Rules 4.17(iv) and 51bis.1(a)(iv))  
 for the purposes of the designation of the United States of America:**

I hereby declare that I believe I am the original, first and sole (if only one inventor is listed below) or joint (if more than one inventor is listed below) inventor of the subject matter which is claimed and for which a patent is sought.

This declaration is directed to the international application of which it forms a part (if filing declaration with application).

This declaration is directed to international application No. PCT/CZ2004/000050 . . . . . (if furnishing declaration pursuant to Rule 26ter).

I hereby declare that my residence, mailing address, and citizenship are as stated next to my name.

I hereby state that I have reviewed and understand the contents of the above-identified international application, including the claims of said application. I have identified in the request of said application, in compliance with PCT Rule 4.10, any claim to foreign priority, and I have identified below, under the heading "Prior Applications," by application number, country or Member of the World Trade Organization, day, month and year of filing, any application for a patent or inventor's certificate filed in a country other than the United States of America, including any PCT international application designating at least one country other than the United States of America, having a filing date before that of the application on which foreign priority is claimed.

Prior Applications: . . . . .  
 . . . . .

I hereby acknowledge the duty to disclose information that is known by me to be material to patentability as defined by 37 C.F.R. § 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the PCT international filing date of the continuation-in-part application.

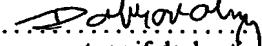
I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name: DOBROVOLNÝ Petr . . . . .

Residence: Brno, Czech Republic . . . . .  
 (city and either US state, if applicable, or country)

Mailing Address: Račerská 779/11, 674 01 Brno, Czech Republic . . . . .

Citizenship: Czech Republic . . . . .

Inventor's Signature:  . . . . .  
 (if not contained in the request, or if declaration is corrected or added under Rule 26ter after the filing of the international application. The signature must be that of the inventor, not that of the agent)

Date: 17. 8. 2004 . . . . .  
 (of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26ter after the filing of the international application)

Name: . . . . .

Residence: . . . . .  
 (city and either US state, if applicable, or country)

Mailing Address: . . . . .

Citizenship: . . . . .

Inventor's Signature: . . . . .  
 (if not contained in the request, or if declaration is corrected or added under Rule 26ter after the filing of the international application. The signature must be that of the inventor, not that of the agent)

Date: . . . . .  
 (of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26ter after the filing of the international application)

☐ This declaration is continued on the following sheet, "Continuation of Box No. VIII (iv)".